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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,226	05/08/2001	Jeffry G. Weers	0073.00	4017

21968 7590 12/21/2005

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,226	WEERS ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8,9,11-15,17-32,44-55,57-62,64,65 and 67-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 8-9, 11-15, 17-32, 44-55, 57-62, 64-65, and 67-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed September 26, 2005 have been entered. Claims 1-5, 8-9, 11-15, 17-32, 44-55, 57-62, 64-65, 67-99 are pending. The outstanding rejection under 35 USC 112, second paragraph is withdrawn in view of the Applicant's remarks.

Double Patenting

The rejection of claims 1-3, 8-9, 11-15, 17-22, 27-32, 44-55, 59-62, 64-65, 67-78 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7-23, 25, 27-30, 34-37, 41-45 of copending Application No. 09/568818 is MAINTAINED for the reasons set forth in the Office Action mailed 7/24/03.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 8-9, 11-15, 17-32, 44-55, 57-62, 64-65, and 67-99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weers et al. (6,309,623) in view of Materne et al. (GB 2065659), references of record.

The instant invention is directed toward a particulate composition comprising particles comprising a saturated, zwitterionic phospholipid and a polyvalent cation at a molar ratio of polyvalent cation to phospholipid of at least 0.05 effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation, wherein the particulate composition is storage stable, and methods of administering such a composition to the pulmonary system of a patient.

Weers et al. teach a stable respiratory dispersion for pulmonary delivery of one ore more bioactive agents comprising a suspension medium having dispersed therein a plurality of perforated microstructures having a mean aerodynnmic diameter of less than

5 micrometers and comprising at least one bioactive agent. The perforated microstructures are taught as comprising 1-90% surfactants, wherein surfactants are selected from saturated phospholipids, nonionic detergents, nonionic block copolymers, ionic surfactants, and combinations thereof. Dipalmitoylphosphatidylcholine is taught as a saturated phospholipid surfactant (saturated, zwitterionic phospholipids, as recited in the instant specification), and poloxamer is taught as a surfactant. Inorganic salts such as calcium chloride are taught as optional excipients, which adjust the pH. Budesonide, fluticasone propionate, salmeterol, and formoterol are taught as bioactive agents that can comprise from 5-90% of the composition. Taught are structural matrices comprising the perforated microstructures, wherein polyvinyl alcohols, polyvinyl pyrrolidones, and polysaccharides are taught as part of the matrix. The perforated microparticles are taught as hollow and/or porous. The suspension medium of the microparticles is taught as a non-aqueous medium. The density of the particles is taught as less than 0.05g/cm3. Taught is administration of the compounds in composition to the lung of a patient in need of such treatment, using a metered dose inhaler. The composition has a gel to liquid crystal phase transition greater than about 40 C. Weers et al. also teaches the mean weighted particle diameter as 0.3 micron Weers et al. also teaches the mixing of the phospholipid composition with the active agents and surfactant composition, followed by the drying process. See Col. 4, line 5-Co1. 8, line 65; Col. 11, lines 25-42; Col. 16, line 28-Col. 20, line 20; Col. 22, lines 44-46; Col. 24, line 56-Co1. 25, line 5; Col. 31, lines 63- col. 32, line 33, for example; Col. 40, line 54- Col. 41, line 55.

Weers et al. lacks an exemplification of a composition comprising saturated phospholipid and divalent cation, and a teaching of the ratio of cation to phospholipid.

Materne teaches calcium phosphatidycholine chloride for pharmaceutical preparations. A ratio of 0.5:1-2:1 of cation to phospholipid is taught. Such as ratio is taught as highly stable for pharmaceutical formulation. See pg. 1, lines 80-129.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to exemplify a suspension medium comprising calcium chloride and dipalmitoylphosphatidyl choline. It would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate the ratio of calcium to dipalmitoylphosphatidyl choline as at least 0.05, as taught by Materne.

One of ordinary skill in the art would have been motivated to formulate a suspension medium comprising calcium chloride and dipalmitoylphosphatidyl choline because Weers et al. exemplify a composition comprising dipalmitoylphosphatidyl choline and they teach that adding salts fine tunes the stabilized dispersions for maximum life and ease of administration.

One of ordinary skill in the art would have been motivated to formulate the ratio of calcium to dipalmitoylphosphatidyl choline as at least 0.05, as taught by Materne because of the expectation of achieving a highly stable pharmaceutical microparticles formulation and because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Since the microparticles taught by the combination of Weers et al. and Materne et al. are the same as those taught by the

instant claims, the microparticles of Weers et al. must have the same gel-to-liquid transition temperatures and storage stability as the microparticles of the instant invention.

Claims 23-25 are directed to a future intended use of the composition. Thus, these claims are not given patentable weight. Claims 79-99 are directed to a composition useful for the purpose of pulmonary delivery and the method of making the same.

The recitation for delivery to the pulmonary system has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Even *arguendo*, Weers et al. teaches the phospholipids composition as useful in pulmonary delivery and therefore, renders the instant claims obvious.

Response to arguments

Applicant's arguments filed September 26, 2005 averring the cited prior art's failure to teach the effect of the polyvalent cation to the phospholipid with regard to the transition crystal temperature have been considered, but are not found persuasive. Examiner notes that the claims are directed to a composition. The cited prior arts

provide motivation to combine the herein recited components into a single composition. Therefore, regardless of the cited prior art teaches the specific properties of the addition of polyvalent cation, the cited prior arts renders the claims obvious

Applicant's arguments filed September 26, 2005 and the declaration by Dr. Weer et al. averring the presence of unexpected results have been considered, but are not found persuasive. Examiner notes that the increased stability by adding polyvalent cation such as calcium salt is actually an expected result, as disclosed by Materne. Furthermore, it is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the superior stability is an expected results. Even *arguendo*, the unexpected benefits are not commensurate with the scope of the subject matter claimed. Only two phospholipids are shown in the declaration and yet, the instant claims encompassed all of the phospholipids. Therefore, the unexpected benefits are not commensurate with the scope of the subject matter recited in the claims.

Applicant's arguments filed September 26, 2005 and the declaration by Dr. Weer et al. averring Materne's teachings are directed to unsaturated phosphatidycholine have

been considered, but are not found persuasive. It is note that nowhere in Materne teaches phosphatidycholine as unsaturated. Such conclusion, i.e., phosphatidycholine taught in Materne as unsaturated, was based on Dr. Weer's speculation. Even if the example used in Materne as unsaturated, it does not exclude the use of cacium salt on saturated phosphatidycholine in Materne since Materne's claims are directed broadly to phosphatidycholine, including both unsaturated and saturated phosphatidycholine (See claims 1-12).

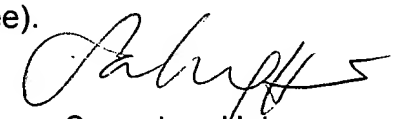
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



San-ming Hui
Primary Examiner
Art Unit 1617